In the Drawings

Please add the enclosed Drawing Figures 9, 10, 11, and 12, that are each provided on a separate sheet.

REMARKS

Applicant has reviewed the Final Office Action mailed February 17, 2006. Claims 12 and 17 are being amended and claims 13-15 are being withdrawn by this Response. Thus, claims 1-12 and 16-18 are pending in the application. Applicant hereby requests further examination and reconsideration of the application in view of the following remarks.

Applicant hereby states that no new matter is being added by the Amendment of claims 12 and 17. Further, the amendments made to claims 12 and 17 are for the correction of mere formalities, clarification of recited elements, do not require further substantive examination and place the application in better condition for allowance.

Specification

The Examiner objected to the amendment filed 11/23/05, stating that Applicant was attempting to add new matter and that there was no indication in the specification that the data was available at the time of filing. Applicant respectfully traverses this objection for the following reasons.

Applicant hereby states that no new matter is being added by the Amendment of the Specification and Drawing Figures. Further, Applicant states that the Amended Specification presented in this Response is the same as that presented in the Response filed November 23, 2005 and the Amended Drawing Figures are the same as that first presented in the Response filed November 23, 2005 and then re-submitted in a Response, to a Notice of Non-Compliant Amendment, filed January 6, 2006.

The disclosure of the existence and detection by the inventors of the instant application of csPCNA within various cancers/cancer cell lines was contained in the application as filed, in particular, the original disclosure in the application on Page 10, Lines 10-17 states:

> The source of the tissue or body fluid is from a subject afflicted with a cancer. The particular cancer is not critical to the present invention. The cancers can be carcinomas, sarcomas, lymphomas, or leukemias. Examples of such cancers include cervical carcinoma, mammary gland carcinoma of ductal or lobular origin, gliomas, prostate, lung, esophageal,

stomach, and ovarian cancer.

(Emphasis added). As disclosed throughout the instant application, the various tissues or body fluid samples containing the various cancers/cancerous cell lines were used because the cancers/cancerous cell lines all contained the csPCNA isoform. The information provided by this Response is merely explanatory and supportive of this original inventive disclosure. FIGS. 9-12 and the description provided for the figures validates the statement made in the original disclosure, that the particular type of cancer is not critical to the present invention because the csPCNA isoform is present/known to exist in all types of cancer. The expression of csPCNA in its acidic isoform is shown to be present in and similar for various cancer cell lines, more particularly FIG. 9 shows its expression in prostate cancer cells, FIG. 10 shows its expression in colon cancer cells, FIG. 11 shows its expression in cervical and brain cancer cells, and FIG. 12 shows its expression in leukemia cells. In each of these figures and the written description it is shown that the acidic csPCNA isoform is found within various cancer cells in a similar form and location. Thus, FIGS. 9-12 merely provide further support to the original disclosure that the type of cancer is not critical because all cancers/cancerous cell lines contain the csPCNAA isoform by showing the presence of the acidic csPCNA isoform in all the various cancer cell lines. Therefore, the acidic csPCNA isoform may be purified from and detected in all the various cancer cells as indicated in the original disclosure. The disclosure provided by the instant application supports the full breadth of the claims of the application as enabling the purification and detection of the acidic csPCNA isoform from various cancer cell lines.

37 CFR §1.132 Declarations

By way of this Response, Applicant is submitting a 37 CFR 1.132 declaration by R. Christopher Rueppell. The declaration and this Response present the amended drawing figures and amended language to the specification that was originally presented in the November 23, 2005 Response and the January 6, 2006 Response, which re-submitted the drawing figures. The declaration evidences proper support of the

amendments to the specification and claims. Because the 35 USC §112, first paragraph rejection is essentially the same as that presented in the June 8, 2005 Office Action Applicant respectfully requests the withdrawal of the current §112, first paragraph rejection.

Applicant is submitting 37 CFR 1.132 declaration from the inventors of the instant application who are declaring themselves as co-inventors of the instant application and co-authors of the article entitled *An Altered form of Proliferating Cell Nuclear Antigen in Various Cancers*, from which proper support of the amendments to the specification and claims, referenced above, is specifically found. The declaration further states that Lori N. Croisetiere, Brian J. Long, Moshe Talpaz and Lawrence Chin who are listed as co-authors of the article are not co-inventors of the instant application.

Applicant is submitting 37 CFR 1.132 declarations from the inventors of the instant application who are declaring themselves as co-inventors of the instant application and co-authors of the article, Tomic et al, Proc. American Assn. For Cancer research, Abstract No. 2507, vol. 42 page 466 (3/01), cited by the Examiner in the rejections below and declaring that P. Wills and C. Lankford who are listed as co-authors of the cited article are not co-inventors of the instant application. These declarations prove that the Tomic reference is the Applicant's own work and cannot be properly cited against the instant application. Since the 35 USC §102 and §103 rejections presented in the current Office Action are essentially the same as those presented in the June 8, 2005 Office Action Applicant respectfully requests the withdrawal of the 35 USC §102 and §103 rejections (described below) based on the Tomic reference.

Objections

The Examiner objected to the Amendment filed on November 23, 2005 as introducing new matter. The Examiner then states that, "[A]pplicant should re-submit this material in declaration form." The Applicant respectfully submits that the 37 CFR 1.132 declaration of R. Christopher Rueppell, more particularly Exhibits A and C, presents the materials of the Amendment in proper form and requests entry of these

materials. Applicant further submits that these materials have been re-printed above in this Response for the convenience of the Examiner.

Claim Rejection -- 35 U.S.C. §112

Claims 12 and 17 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that claim 12 is confusing because it is not clear if the terminology "is used to produce antibodies..." is to be another step or intended use. The Examiner states that the dependency of claim 17 is unclear. Applicant respectfully submits that the amendment of claims 12 and 17 obviate these rejections and place these claims in condition for allowance. Therefore, Applicant respectfully requests withdrawal of the §112, second paragraph rejection.

The Examiner states that claims 1-11 and 16-18 were rejected under 35 U.S.C. §112, first paragraph, because the specification for the reasons of record in the paper mailed 6/8/05. Examiner further states that the "[A]pplicant provided additional data in the form of drawings to overcome this rejection. The material needs to be presented in the form a declaration under 37 CFR 1.132. If presented in such a form, then the rejection would be overcome."

Applicant respectfully submits that the 37 CFR 1.132 declaration of R. Christopher Rueppell, enclosed herein, and more particularly Exhibit A of the declaration presents the drawing figures and Exhibit C of the declaration presents the written description of the drawing figures in Exhibit A in the appropriate and requested form. Applicant submits that the drawing figures 9-12 have been re-printed above in this Response for the Examiner's convenience.

The Applicant has re-printed the traversing arguments, originally presented in the Response filed on November 23, 2005 to the 112, first paragraph rejection, for the Examiner's convenience. The 112 rejection stated that while being enabling for the purification and detection of breast cancer specific PCNA, does not reasonably provide enablement for the purification and detection of any cancer-specific PCNA. The Applicant traverses this rejection for the reasons provided above and for the following

reasons.

"Adequate description under the first paragraph of 35 U.S.C. 112 does not require literal support for the claimed invention. . . . Rather, it is sufficient if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed" *Ex parte Parks,* 30 USPQ2d 1234, 1236-37 (B.P.A.I. 1993). The instant specification teaches to the identification of the presence of csPCNA in all malignant cells, states that this unique isoform of the PCNA protein exists in all cancerous cells regardless of the particular type of cancer (Page 10, Lines 10-17), and provides an example of how such a unique form of the PCNA protein is isolated, purified, and detected. One of ordinary skill in the art would readily recognize not only the conceptual foundation of the instant invention but the practical guidance for the isolation, purification, and detection as providing proof of the possession of the instant invention including the breadth of the disclosure provided and claimed. Thus, Applicant respectfully requests withdrawal of the §112, first paragraph rejection and allowance of claims 1-8.

Further, even in unpredictable arts, a specification need not disclose every example or species covered by a claim:

> To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples .... more importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid "literal" infringement of such claims by merely finding another analogous catalyst complex which could be used" *In re Angstadt,* 190 USPQ at 218.

In the instant application the disclosure of the csPCNA isolation, purification and detection from a line of breast cancer cells provides more than sufficient enablement to one of ordinary skill in the art. The application of the various procedural steps taken and described in the specification would allow one to make and use the present invention across the broad spectrum of cancer types claimed and described by the instant application.

The Examiner cites Tomic et al, Proc. American Assn. For Cancer research, Abstract No. 2507, vol. 42 page 466 (3/01) (hereinafter "Tomic"), for the proposition that the acidic form of PCNA detectable by XPG is specific for breast cancer cells. Further, the Examiner states that applicant's own specification (page 3) discloses the csPCNA is specific for breast cancer cells. Applicant respectfully submits that the Examiner has misinterpreted both the Tomic reference and the specification. Neither Tomic or the specification (page 3) state that the acidic form of PCNA (csPCNA) is specific to breast cancer cells alone. Tomic and the specification (page 3) state that in malignant (cancerous) cells the acidic form of PCNA exists and can be detected and that in non-malignant cells csPCNA does not exist. The example (cell type) used to form the basis of proof for this was malignant/non-malignant breast cells, in the Tomic reference. However, the instant application originally disclosed that the particular tissue or body fluid, source of tissue or body fluid, and even the type of cancer is not critical because the csPCNA isoform exists in all cancerous cell lines/types, regardless. Such a statement in the instant application is not one of mere unsupported conclusory logic but had been arrived at through painstaking and novel inventive industry by the inventors of the instant application as is reflected in the works cited by the Examiner and referenced in the 37 CFR §1.132 Declarations being submitted herein. Thus, the amended disclosure is merely providing the supportive, background framework within which the instant application must be interpreted. Thus, Applicant respectfully submits that the full breadth of the claims presented by the instant application is and has been properly supported from the original filing of the application.

With the csPCNA identified as existing in only malignant cell types, the number of examples used to illustrate the invention is irrelevant as indicated by the specification which states:

> The source of the tissue or body fluid is from a subject afflicted with a cancer. The particular cancer is not critical to the present invention. The cancers can be carcinomas, sarcomas, lymphomas, or leukemias. Examples of such cancers include cervical carcinoma, mammary gland carcinaoma of ductal or lobular origin, gliomas, prostate, lung, esophageal, stomach, and ovarian cancer.

(Page 10, Lines 10-17). In each cancer type the csPCNA exists and can be isolated,

purified, and detected utilizing the methods and techniques claimed by the instant application and described in the specification which are well known to those of ordinary skill in the field of art. For all of the above reasons, Applicant respectfully requests the withdrawal of the §112, first paragraph rejection and allowance of claims 1-8.

Claim Rejection – 35 U.S.C. §102

Claims 4-5, 9-10, and 16-17 were rejected under 35 U.S.C. §102(a) as being anticipated by Tomic et al, Proc. American Assn. For Cancer research, Abstract No. 2507, vol. 42 page 466 (3/01) (hereinafter "Tomic") as evidence by Gary et al JBC vol. 272 p. 24522 (1997) (hereinafter "Gary"). Applicant respectfully submits that the 37 CFR 1.132 declarations submitted by Robert J. Hickey, Linda H. Malkas, Lauren Schnaper, Derek Hoelz, and Dragana Tomic overcome this rejection by proving that the Tomic reference is in fact Applicant's own work and that inventorship has been properly determined and presented to the USPTO.

For the convenience of the Examiner, Applicant has re-printed, in substantial similarity, the traversing argument originally presented in the November 23, 2005 Response. Applicant respectfully traverses this rejection for the reasons stated above with respect to the §112, first paragraph rejection and for the following reasons.

"One's own work may not be considered prior art in the absence of a statutory basis," *Riverwood Int'l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 6 USPQ2d 1331, 1338 (Fed. Cir. 2003). Tomic is an abstract that is authored by L.H. Malkas (aka., Linda H. Malkas), R.J. Hickey (aka., Robert J. Hickey), D.J. Hoelz (aka., Derek J. Hoelz), L. Schnaper (aka., Lauren Schnaper), and D. Tomic (aka., Dragana Tomic), which are all listed inventors and applicants on the instant application. Therefore, §102(a) is an invalid rejection because the invention was **not** known or used **by others** in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, as required by this statutory rejection.

Further, there is no valid §102(b) rejection because the invention was **not** patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, as required by this statutory rejection. The filing date of the

instant application is February 27, 2002 and the publication date of the Tomic reference, as stated by the Examiner in the current Office Action, is at the earliest March 1, 2001. Since the filing date is less than twelve months (one year) from the date of publication for the Tomic reference the Tomic reference does not qualify as a valid rejection under §102(b).

For these reasons, Applicant respectfully submits that the Tomic reference must be withdrawn as a prior art reference because it is the work of the inventors/applicants of the instant application and it does not provide a statutory basis for rejection. Therefore, Applicant respectfully requests the withdrawal of the §102(a) rejection, since there is no longer any prior art basis for such a rejection, and allowance of claims 4-5, 9-10, and 16-17.

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *W.L. Gore & Assocs. v. Garlock*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Further, "anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, arranged as in the claim." *Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 221 USPQ 481, 485 (Fed. Cir. 1984) (citing *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983)) (emphasis added).

With respect to the Gary reference, the Examiner references Gary for disclosing the detection of csPCNA through the binding of XPG. The Examiner is correct in that Gary does identify that a specific region of PCNA interacts with XPG, a homolog of FEN1, which was disclosed in the specification of the instant application on Page 4, Line 29, through Page 5, Line 6. Thus, Gary is properly determined to make a generic disclosure of a general method for detecting the presence of PCNA. However, the isolation, purification, and detection of the presence of the csPCNA isoform in malignant cells, as recited in claims 1 and 4, respectively, of the instant application, is not disclosed by Gary. It is also noted, that since Tomic is an invalid reference and cannot be considered, the Gary reference does not provide a basis for a §102(a) rejection. Therefore, Applicant respectfully requests the withdrawal of the §102(a) rejection with respect to the Gary reference and submits that claims 1-8 are in condition for allowance.

Claim Rejection -- 35 U.S.C. §103

Claims 4-11 and 16-17 were rejected under 35 U.S.C. §103(a) as being unpatentable under Tomic in view of Gary and US Patent 6,514,713 ("Knott"). Applicant respectfully submits that the 37 CFR 1.132 declarations (included herein) by the inventors of the current invention prove that the Tomic reference is the Applicant's own work. For the reasons stated above with respect to the §112, first paragraph and §102(a) rejection the Applicant respectfully traverses the §103(a) rejection.

It is Applicant's belief that the Examiner's identification of Knott et al as US 6,514,703 was a typographical error and that in fact US Patent 6,514,713 was what the Examiner intended to enter. Applicant further traverses this rejection for the following reasons.

The Knott reference, and the Gary reference for the reasons stated above, both fail to disclose the isolation, purification, and detection of csPCNA found in malignant cells, as recited by claims 1 and 4, respectively, of the instant invention. Knott discloses a method for detecting the presence of the mutated BRCA1 gene that can be found in various types of cancer cells. This is not the current invention or the invention claimed in the instant application. Therefore, Applicant respectfully requests the withdrawal of the §103(a) rejection and allowance of claims 4-8.

"If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue." *In re Rouffet*, 149 F.3d 1350, 47 USPQ2d 1453, 1457 (Fed. Cir. 1998). Looking at the argument presented by the Examiner, it appears that the Examiner is attempting to use Gary's general disclosure of XPG interacting with PCNA and Knott's disclosure of an ELISA for the detection of breast cancer to arrive at the instant invention which teaches to the isolation, purification, and detection of csPCNA which is found in all cancer types. This line of reasoning would appear to lead to the conclusion that since XPG interaction is known and ELISA detection is known, any invention utilizing either or both of these features is inherently unpatentable. To follow the Examiner's argument to its logical conclusion the public policy of the patent system, encouraging inventive endeavors through granting of limited

time, exclusionary protections, would be thwarted. Therefore, because Gary and Knott either alone or in combination do not disclose, teach, or suggest the method of isolating, purifying, and detecting csPCNA in various cancer cell lines as recited in the claims of the instant invention, Applicant respectfully requests withdrawal of the §103 rejection and allowance of claims 4-8.

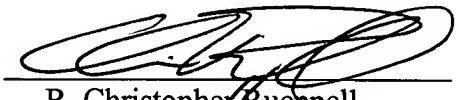
CONCLUSION

In light of the forgoing, reconsideration and allowance of the claims is earnestly solicited. Accordingly, notification to that effect is earnestly requested. In the event that issues arise in the application which may readily be resolved via telephone, the Examiner is kindly invited to telephone the prosecuting attorney, identified below, at (410) 347-8754 to facilitate prosecution of the application.

Respectfully submitted,

Linda H. Malkas,

Dated: August 16, 2006

By: 
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